

Version of Amended Specification Paragraphs With Markings to Show Changes**Made:**

NOTE: Insertions are marked by underlining and bold text.

Please replace the last paragraph on page 3 (which wraps around to the top of page 4) with the following paragraph:

Despite their sequence variations, all five subfamilies of the Ras superfamily share conserved structural features. Four conserved sequence regions (motifs I-IV) have been studied in the LMW GTP-binding proteins. Motif I is the most variable but has the conserved sequence, GXXXXGK (**SEQ ID NO:34**). The lysine residue is essential in interacting with the .beta.- and .gamma.-phosphates of GTP. Motif II, III, and IV contain highly conserved sequences of DTAGQ (**SEQ ID NO:35**), NKXD (**SEQ ID NO:36**), and EXSAX (**SEQ ID NO:37**), respectively. Specifically, Motif II regulates the binding of gamma-phosphate of GTP; Motif III regulates the binding of GTP; and Motif IV regulates the guanine base of GTP. Most of the membrane-bound LMW GTP-binding proteins generally require a carboxy terminal isoprenyl group for membrane association and biological activity. The isoprenyl group is added posttranslationally through recognition of a terminal cysteine residue alone or a terminal cysteine-aliphatic amino acid-aliphatic amino acid-any amino acid (**CAAX; SEQ ID NO:38**) motif. Additional membrane-binding energy is often provided by either internal palmitoylation or a carboxy terminal cluster of basic amino acids. The LMW GTP-binding proteins also have a variable effector region, located between motifs I and II, which is characterized as the interaction site for guanine nucleotide exchange factors (GEFs) or GTPase-activating proteins (GAPs). GEFs induce the release of GDP from the active form of the G protein, whereas GAPs interact with the inactive form by stimulating the GTPase activity of the G protein.

Please replace the last full paragraph on page 4 with the following paragraph:

D2
A number of Rho GTP-binding proteins have been identified in plasma membrane and cytoplasm. These include RhoA, B and C, and D, rhoG, rac 1 and 2, G25K-A and B, and TC10 (Hall, A. et al. (1993) Philos. Trans. R. Soc. Lond. (Biol.) 340:267-271). All Rho proteins have a CAAX (SEQ ID NO:38) motif that binds a prenyl group and either a palmitoylation site or a basic amino acid-rich region, suggesting their role in membrane-associated functions. In particular, RhoD is a protein that functions in early endosome motility and distribution by inducing rearrangement of actin cytoskeleton and cell surface (Murphy, C. et al. (1996) Nature 384:427-432). During cell adhesion, the Rho proteins are essential for triggering focal complex assembly and integrin-dependent signal transduction (Hotchin, N. A. and Hall, A. (1995) J. Cell Biol. 131:1857-1865).

Please replace the last paragraph on page 4 (which wraps around to the top of page 5) with the following paragraph:

D3
The Ras subfamily proteins already indicated supra are essential in transducing signals from receptor tyrosine kinases (RTKs) to a series of serine/threonine kinases which control cell growth and differentiation. Mutant Ras proteins, which bind but cannot hydrolyze GTP, are permanently activated and cause continuous cell proliferation or cancer. TC21, a Ras-like protein, is found to be highly expressed in a human teratocarcinoma cell line (Drivas, G. T. et al. (1990) Mol. Cell. Biol. 10: 1793-1798). Rin and Rit are characterized as membrane-binding, Ras-like proteins without the lipid-binding CAAX (SEQ ID NO:38) motif and carboxy terminal cysteine (Lee, C.-H. J. et al. (1996) J. Neurosci. 16: 6784-6794). Further, Rin is shown to localize in neurons and have calcium-dependant calmodulin-binding activity.